IDENTIFYING FUNCTIONAL LINKS BETWEEN THE IMMUNE SYSTEM AND BRAIN FUNCTION INCLUDING BEHAVIOR

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PARTICIPATING INSTITUTES AND CENTERS (ICs):

National Institute of Mental Health
(http://www.nimh.nih.gov/)
National Institute of Neurological Disorders and Stroke
(http://www.ninds.nih.gov/)
National Institute on Drug Abuse
(http://www.nida.nih.gov/)
National Institute of Arthritis and Musculoskeletal and Skin Diseases
(http://www.niams.nih.gov/)

THIS PA CONTAINS THE FOLLOWING INFORMATION

PURPOSE OF THIS PA

The Program Announcement replaces PA-93-009.

The National Institute of Mental Health (NIMH), National Institute on Neurological Disorders and Stroke (NINDS), National Institute on Drug Abuse (NIDA), and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) request research grant applications to study neuroimmune molecules and mechanisms involved in regulating normal and pathological central nervous system (CNS) function. Areas of research interest include those raised in discussions at the recent workshop "Strategies for Identifying Functional Links Between the Immune System, Brain Function, and Behavior" http://www.nimh.nih.gov/research/linkssummary.cfm. This program announcement (PA) also incorporates topics explored at the "Research Roundtable on Pediatric Autoimmune europsychiatric Disorders Associated with Streptococcus (PANDAS)" http://www.nimh.nih.gov/research/pandassummary.cfm.

RESEARCH OBJECTIVES

Background

Immune molecules such as cytokines, chemokines, and growth factors and immune cells can modulate brain function through multiple signaling pathways originating from peripheral and CNS cells. Immunological, physiological and psychological stressors can engage cytokines and other immune molecules in bi-directional interactions with brain neuroendocrine, peptide, and neurotransmitter systems. For example, brain cytokine levels increase following stress exposure, and treatments that decrease the impact of stress on behavior also reverse stress-mediated effects on cytokines.

Cytokines and chemokines can also modulate CNS function in the absence of overt immunological, physiological, or psychological challenges. For example, cytokines and cytokine receptor inhibitors affect cognitive and emotional processes. Recent evidence suggests that immune molecules modulate brain systems differently across the lifespan. Cytokines and chemokines regulate neurotrophins and other molecules critical to neurodevelopmental processes, and exposure to certain neuroimmune challenges early in life affects brain development. In adults, cytokines and chemokines affect synaptic plasticity and other ongoing neural processes. Finally, interactions of immune molecules with the hypothalamic-pituitary-gonadal system indicate that sex differences are a significant factor determining the impact of neuroimmune influences on brain function and behavior.

Research Scope

The potent effects of cytokine molecules in the brain are mediated through multiple signaling pathways. However, details regarding the extent, routes, or mechanisms whereby immune signaling molecules affect the brain in either normal conditions or during immune challenge are largely unexplored. The purpose of this PA is to identify research themes that may help to bridge the gap in understanding how immune mediators affect brain function and behaviors related to cognition and mood. This includes studies of the effects of immune molecules and cells on molecular and cellular neural processes, neuronal signaling, glial-neural interactions, neural activation, and objective behavioral endpoints of relevance to mood, cognition, and motivation. Studies examining immune molecule effects on neurodevelopment and across the lifespan as well as studies comparing effects in males and females are also encouraged. It should be noted that studies aimed at examining how the brain or stressors affect peripheral immune function are not appropriate for this solicitation. Similarly, studies of immune cell entry and fate in brain are appropriate only if they examine how these cells affect ongoing brain processes and/or behavior.

Areas of interest

Development and extension of research tools to examine how immune molecules affect CNS function and behavior:

o Develop and characterize cytokine receptor selective ligands.

o Develop genetic tools to alter selective components of the immune system and brain signaling pathways within limited developmental periods.

o Identify sensitive markers for determining the effects of pre- and post-natal infection on normal brain development.

o Develop neuroimaging tools for studying cytokine effects within specific brain regions.

o Develop non-invasive tools for examining blood/brain barrier permeability to immune molecules and cells and antibodies.

o Develop long-term markers of immune response activation in brain.

Development and extension of animal models of immune signaling in brain:

o Model chronic therapeutic administration of cytokines as used in chemotherapy to examine the mechanisms responsible for effects on mood and cognition.

o Develop and refine models to examine the potential effects of pre- and post-natal infection on brain development and adult brain function and behavior.

o Model effects of acute and chronic immune challenge on neuroendocrine systems, neurochemistry, electrophysiology, molecular signaling, and gene expression in neurons.

o Model neural effects of autoantibodies and other immune molecules implicated in autoimmune disorders affecting mental health.

o Examine the potential role of abnormalities of the blood/brain barrier in determining neuroimmune responses.

Identification of pathways mediating effects of peripheral and central immune activation on brain:

o Identify and characterize receptors and signal transduction mechanisms responsible for cytokine and chemokines actions in brain.

o Identify factors regulating brain cytokine and chemokine expression, release, and degradation.

o Determine the role of neurotransmitters, neuropeptides, and neurohormones as potential mediators and/or modulators of cytokine and chemokines expression and signaling.

o Examine effects of cytokines and chemokines on gene expression and activation of neurotransmitters, neurohormones, and other signaling molecules in brain.

o Elucidate the role of cytokines and chemokines as modulators of neural-glial communication.

o Examine interactions of cytokines and chemokines with acute and chronic psychoactive drugs at molecular, cellular, and behavioral levels.

Examination of genetic determinants of immune responses in brain:

o Model genetic variations of immune molecule expression as potential susceptibility factors for developing neuropsychiatric symptoms.

o Examine combined effects of stress and/or adverse early environmental experience with genetic alterations in immune signaling in predisposing patterns of brain development and behavior.

o Examine the impact of gene deletion of cytokines/chemokines and their receptors, neurotransmitters, peptides, receptors, hormones, or other signaling molecules on cytokine actions in brain.

Identification of effects of cytokines/chemokines on brain function across the lifespan:

o Examine the developmental expression of cytokines, chemokines, receptors, and related signaling molecules in brain.

o Examine the development of blood brain barrier function and the neurobiological impact of developmentally mediated changes in immune molecule infiltration of brain.

o Determine the effects of cytokines and chemokines on stem cell production and fate.

o Examine the long-term consequences of acute and chronic infection throughout the lifespan on susceptibility to adverse physiological and psychological effects of stress.

Delineation of the physiological/behavioral actions of cytokines/chemokines:

o Examine the impact of immune molecules in well-characterized cellular and behavioral model systems. Examples of areas of study might include neural plasticity, circadian activity, sleep, learning, conditioned fear, eating, memory, maternal behavior, or sexual behavior.

o Identify peripheral to brain and/or central pathways mediating specific behavioral effects of cytokines and chemokines.

o Identify brain regions, cell types, receptors and signaling pathways mediating specific behavioral effects of cytokines and chemokines.

Clinical applications:

o Employ functional imaging in both basic and clinical studies to determine the effects of individual cytokines and more complex, infection or autoimmune-related immune challenges on brain function.

o Develop parallel measures of cytokine/chemokines action in clinical and basic neuroscience studies.

o Enhance translational efforts to identify cellular and neurochemical mediators responsible for neuropsychiatric symptoms associated with naturally occurring conditions of immune compromise or cytokine therapy.

o Develop more sensitive measures of peripheral immune cytokine/chemokine status and identify ways to relate peripheral to brain concentrations of immune molecules.

o Identify surrogate markers of CNS impact of infection and autoimmune disorders.

o Explore comorbidity of immune system deregulation with mental disorders.

o Search for, identify and characterize possible autoantibodies and their target molecules in animal models and in neuropathological studies using clinical brain and CSF samples from Sydenham's Chorea patients and other psychiatric populations of suspected autoimmune origin.

The NIAMS solicits applications to study immune-CNS interactions in rheumatic diseases. Rheumatic diseases such as systemic lupus erythematosus (SLE) and rheumatic arthritis (RA) are autoimmune diseases whose clinical manifestation often include intermittent or progressive neuropsychiatric dysfunction, including depression, memory loss, concentration deficits, dementia, and anxiety syndromes. In general, a fluctuating course of disease rather than a rapid decline to dementia is characteristic. Cognitive impairment can occur in isolation or in the context of other neurologic or psychiatric syndromes such as depression or psychosis. Certain deficits are specifically associated with particular serum autoantibodies. For example, recent reports have shown lupus psychosis to be associated with the presence of antibodies directed against the carboxyl terminus of the ribosomal P proteins, and a shared amino acid sequence between HLA-DQB1 and P peptides was strongly associated with anti-P antibodies in SLE, suggesting the presence of autoreactive T cells directed against P proteins. The mechanisms explaining these associations and their contribution to disease pathogenesis are uncertain. Research in these areas could improve significantly with the development of new techniques and

with the development of new animal models to explore the pathogenesis of cognitive and psychiatric disorders in the rheumatic diseases.

Examples of areas of NIAMS interest include, but are not limited to:

o Studies designed to discover the links between immune dysfunction and nervous system involvement in RA, SLE, scleroderma, and other rheumatic diseases, including studies in new and existing animal models of disease.

o Hypothesis-generating studies of murine and human neuropsychiatric SLE to examine the role of inflammatory mediators and inflammation of the central nervous system and/or its vasculature in NP-SLE pathophysiology, e.g., endothelial activation, immune complex deposition and effacement of the blood-brain barrier, pericyte and microglial activation, abnormalities in neurotransmission and neurophysiology, autoantibodies such as antiphospholipid antibodies, etc.

o Assessment of structural and functional aspects of the nervous system in rheumatic diseases (i.e., by neuroimaging or neuropathology).

o Evaluation of prospective biomarkers of CNS involvement in rheumatic disease, including biological, imaging, and other modalities that reflect normal or abnormal neuro-immune processes.

o Neurobehavioral evaluation of murine models of SLE.

o Evaluation of neurobehavioral effects secondary to treatment of rheumatic disease.

MECHANISM OF SUPPORT

This PA will use the National Institutes of Health (NIH) research project grant (R01), Small Grant (R03), and Exploratory/Developmental grant (R21) award mechanisms. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. The total project period for a new or competing R01 application submitted in response to this PA may not exceed five years. The Small Grant (R03) provides two years of funding with a maximum of $50,000 direct costs for each year.

Exploratory/Developmental Grants (R21) submitted in response to this PA will use the guidelines established by NIMH

(http://grants.nih.gov/grants/guide/pa-files/PA-00-073.html. The R21 mechanism will provide up to three years of funding with a maximum of $125,000 direct costs for each year. The objective of the R21 mechanism is to encourage applications for one-time grants to support innovative research requiring preliminary testing or development, exploration of the use of approaches and concepts new to a particular substantive area, research and development of new technologies, techniques or methods, or initial research and development of a body of data upon which significant future research may be built.

Instructions and information for the Small Grant Program (R03) are found at: http://grants.nih.gov/grants/guide/pa-files/PAR-99-140.html. Special instructions and information for the Exploratory/Development Grants (R21) may be found at: http://grants.nih.gov/grants/guide/pa-files/PA-00-073.html.

This PA uses just-in-time concepts. It also uses the modular as well as the non-modular budgeting formats (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, if you are submitting an application with direct costs in each year of $250,000 or less, use the modular format. Otherwise follow the instructions for non-modular research grant applications.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

o For-profit or non-profit organizations o Public or private institutions, such as universities, colleges, hospitals, and laboratories
o Units of State and local governments
o Eligible agencies of the Federal government
o Domestic or foreign
o Faith-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity answer questions from potential applicants. Inquiries may fall into two areas: scientific/research and financial or grants management issues:

o Direct your questions about scientific/research issues to:

Lois Winsky, Ph.D.
Division of Neuroscience and Basic Behavioral Research
National Institute of Mental Health
6001 Executive Boulevard, Room, 7184, MSC 9641
Bethesda, MD 20892-9641
Telephone: (301) 443-5288
FAX: (301) 402-4740
Email: lois@helix.nih.gov

Ursula Utz, Ph.D.
Program Director, Neural Environment
National Institute of Neurological Disorders and Stroke
6001 Executive Boulevard, Room 2134
Bethesda, MD 20892-9521
Telephone: (301) 496-1431
FAX: (301) 480-2424
Email: utzu@ninds.nih.gov

Charles Sharp, Ph.D.
Division of Neuroscience and Behavior Research
National Institute on Drug Abuse
6001 Executive Boulevard, Room 4269
Bethesda, MD 20892
Telephone: (301) 435-1887
FAX: (301) 594-6043
Email: csharp@ngmsmtp.nida.nih.gov

Deborah N. Ader, Ph.D.
Director, Behavioral and Prevention Research Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases

45 Center Drive, Building 45, Room 5A19H
Bethesda, MD 20892-6500
Telephone: (301) 594-5032
FAX: (301) 480-4543
Email: aderd@mail.nih.gov

o Direct your questions about financial or grants management matters to:

Carol Robinson
Grants Management Branch
National Institute of Mental Health
6001 Executive Boulevard, Room 6115, MSC 9605
Bethesda, MD 20892-9605
Telephone: (301) 443-3858
FAX: (301) 443-6885
Email: Crobinso@mail.nih.gov

James Washington
Grants Management Branch
National Institute of Neurological Disorders and Stroke
6001 Executive Boulevard, Room 3290, MSC 9537
Bethesda, MD 20892-9537
Telephone: (301) 496-9231
FAX: (301) 402-0219
Email: Washingj@ninds.nih.gov

Gary Fleming, J.D., M.A.
Grants Management Branch
National Institute on Drug Abuse
6001 Executive Boulevard, Room 3131, MSC 9541
Bethesda, MD 20892-9541
Telephone: (301) 443-6710
FAX: (301) 443-6847
Email: gf6s@nih.gov

Melinda Nelson
Grants Management Officer

National Institute of Arthritis and Musculoskeletal and Skin Diseases
45 Center Drive, Natcher Building, Room 5A49F
Bethesda, MD 20892-6500
Telephone: (301) 594-3535
FAX: (301) 480-5450
Email: nelsonm@mail.nih.gov

The National Institute on Aging (NIA) has overlapping interests in the scientific areas covered by this announcement and welcomes R01 and R03 applications. For further information, applicants may contact NIA program staff:

Andrew A. Monjan, Ph.D., M.P.H.
National Institute on Aging
7201 Wisconsin Avenue, Suite C3C07
Bethesda, MD 20892
Telephone: (301) 496-9350
FAX: (301) 496-1494
Email: am39m@nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at http://grants.nih.gov/grants/dates.htm. Application deadlines are also indicated in the PHS 398 application kit.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to $250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at

http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

SPECIFIC INSTRUCTIONS FOR APPLICATIONS REQUESTING $500,000 OR MORE PER YEAR:
Applications requesting $500,000 or more in direct costs for any year must include a cover letter identifying the NIH staff member within one of NIH institutes or centers who has agreed to accept assignment of the application.

Applicants requesting more than $500,000 must carry out the following steps:

1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as you are developing plans for the study;

2) Obtain agreement from the IC staff that the IC will accept your application for consideration for award; and,

3) Identify, in a cover letter sent with the application, the staff member and IC who agreed to accept assignment of the application.

This policy applies to all investigator-initiated new (type 1), competing continuation (type 2), competing supplement, or any amended or revised version of these grant application types. Additional information on this policy is available in the NIH Guide for Grants and Contracts, October 19, 2001 at
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040, MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be received by or mailed before the receipt dates described at http://grants.nih.gov/grants/funding/submissionschedule.htm.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. An appropriate scientific review group convened in accordance with the standard NIH peer review procedures (http://www.csr.nih.gov/refrev.htm) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

o Receive a written critique
o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
o Receive a second level review by the appropriate national advisory council or board

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

o Significance
o Approach
o Innovation
o Investigator
o Environment

The scientific review group will address and consider each of these criteria in assigning your application's overall score, weighting them as appropriate for each application. Your application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, you may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

(1) SIGNIFICANCE: Does your study address an important problem? If the aims of your application are achieved, how do they advance scientific knowledge? What will be the effect of these studies on the concepts or methods that drive this field?

(2) APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Do you acknowledge potential problem areas and consider alternative tactics?

(3) INNOVATION: Does your project employ novel concepts, approaches or methods? Are the aims original and innovative? Does your project challenge existing paradigms or develop new methodologies or technologies?

(4) INVESTIGATOR: Are you appropriately trained and well suited to carry out this work? Is the work proposed appropriate to your experience level as the principal investigator and to that of other researchers (if any)?

(5) ENVIRONMENT: Does the scientific environment in which your work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, your application will also be reviewed with respect to the following:

PROTECTIONS: The adequacy of the proposed protection for humans, animals, or the environment, to the extent they may be adversely affected by the project proposed in the application.

INCLUSION: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria included in the section on Federal Citations, below)

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

REQUIRED FEDERAL CITATIONS

MONITORING PLAN AND DATA SAFETY AND MONITORING BOARD: Research components involving Phase I and II clinical trials must include provisions for assessment of patient eligibility and status, rigorous data management, quality assurance, and auditing procedures. In addition, it is NIH policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks (NIH Policy for Data Safety and Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the AMENDMENT "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html);
a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.
The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and

ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance Nos. 93.242 (NIMH), 93.853 (NINDS), 93.279 (NIDA), and 93.846 (NIAMS). Awards are made under authorization of sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies and Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Return to Volume Index
Return to NIH Guide Main Index